

Serial No.: 09/766,399

Group Art Unit: 1634

ISSUES

Claims 2-16 are rejected under 35 U.S.C. §112, first paragraph, enablement, in that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

Claims 2-16 are rejected under 35 U.S.C. §102(b) as being anticipated by Ishige *et al.* (EP 0754757 A2).

REMARKS

Substantial Duplication under 37 CFR 1.75:

The Examiner submits that Claims 7 and 8 are substantially duplicative. Applicant has canceled claim 7, without prejudice.

The First Paragraph of Section 112 Rejection of Claims 1-6 and 25-36: Enablement

Claims 2-16 are rejected under 35 U.S.C. §112, first paragraph, enablement, in that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

The Examiner asserts that the ability of a promoter to function is highly sequence specific and that the art teaches that mutations in a critical region of a promoter element can destroy the ability of a construct to function in promotion. The Examiner further asserts that it is evident that it is highly unpredictable how promoter elements will respond to even very minor sequence changes. The Examiner also

Serial No.: 09/766,399

Group Art Unit: 1634

states that there is no clear pattern as to which sets of elements work or how to predict on its face if a set of elements will be able to promote expression. Also, she states that the specification does not provide any guidance as to how the elements can be rearranged, and still result in a functional promoter, and that the specification does not provide any guidance as to what number of intervening sequences can be placed between the recited elements and still result in a functional promoter. The Examiner concludes that in light of the sequence specificity required for promoter activity, the high degree of unpredictability of functionally variant promoter sequences, that the specification does not provide necessary guidance as to how to modify the claimed sequences and retain functional promoter elements. The Examiner states that the rejection is particularly applied to address claims which require the elements recited in claim 2(a) with any possible intervening sequences and sequences that hybridize or have 90% homology to 2(a) or 2(b).

Applicant respectfully traverses. The standard for enablement has been well characterized by the Federal Circuit decisions in multiple court cases:

" [A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of §112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support...." "[A]ny party making the assertion that a U.S. patent specification or claims falls, for one reason or another, to comply with §112 bears the burden of persuasion in showing said lack of compliance."

Fiers v. Sugano, 984 F.2d 1164, 25 USPQ 2d 1601, 1607 (Fed. Cir. 1993) (quoting *In re Marzocchi*, 439 F.2d. 220, 223, 169 USPQ 367, 369 (C.C.P.A. 1971); *Weil v. Fritz*, 601 F.2d 551, 555, 202 USPQ 447, 450 (C.C.P.A. 1979))

In *re Moore*, 439 F.2d. at 1235-36, 169 USPQ at 238-39 (C.C.P.A. 1971) the CCPA summarized the general requirements for an enabling disclosure: "The relevant inquiry may be summed up as being whether the scope of enablement

Serial No.: 09/766,399
Group Art Unit: 1634

provided to one of ordinary skill in the art by the disclosure is such as to be commensurate with the scope of protection sought by the claims."

In *re* Angstadt, 5327 F.2d 498, 190 USPQ 214 (C.C.P.A. 1976), the CCPA determined that the specification did not disclose every catalyst that would work or every catalyst that would not work. The CCPA held that even in unpredictable arts, the specification need not disclose every example or species covered by a claim:

To require such a complete disclosure would apparently necessitate a patent application or applications with "thousands" of examples or the disclosure of "thousands" of catalysts.... More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiment. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid "literal" infringement of such claims by merely finding another analogous catalyst complex which could be used..."

In *re* Angstadt, 5327 F.2d 498, 190 USPQ 214 (C.C.P.A. 1976)

Thus, Angstadt teaches that when the application contains a list of catalysts and taught how to make and use them, the experimentation required to determine which catalysts produced the asserted results was not overly burdensome. It is respectfully submitted that the specification is not required to disclose all possible permutations defined by the limitations of claims 2-16. The specification is required to provide sufficient disclosure and enablement so that one skilled in the art could make the embodiments encompassed by the claims.

The specification is clear regarding what is meant by "synthetic multimeric promoter element region" or SMPER. On page 4, lines 24-33 of the specification it states that a synthetic multimeric promoter element region is: "a nucleic acid having a nucleotide sequence comprising more than one promoter element, wherein the arrangement of the multimeric combination of the promoter elements is not found in nature." The claims are supported in the present specification where the modification of the SMPER sequence is taught, for example at pages 11 through 14.

Serial No.: 09/766,399
Group Art Unit: 1634

The individual promoters and their elements and methods for synthesizing and isolating the plant promoters, as well as testing for functionality of the invention are provided in the Figures 1, and 7-14, and Examples 1 through 4 of the present application.

Applicant submits that the instant specification enables one of skill in the art to make and use a SMPER capable of driving transcription in a plant cell. Applicant has noted Examiner's comment regarding the claim language of 2(a), and has amended the claim to include sequences not more than 2000 nucleotides in length. Additionally, 2KB is a very appropriate putative promoter length as handled by one of skill in the art. As the amended claim 2(a) now includes only those sequences capable of driving transcription in a plant cell, comprising the claimed subunits sequentially arranged, across a total nucleotide sequence length of not more than 2000 nucleotides, this in turn limits the size of intervening sequences. Applicant respectfully submits that it would be well known to one of skill in the art the process of analyzing sequences to determine which had 90% identity as determined by the GAP algorithm under default parameters across the entire length of the claimed SEQ ID NO.: 65 or to the promoter elements as described in claims 2, 8, and 12.

One of skill in the art would find the specification as written and as illustrated in Figures 1 through 14, discloses a list of functional SMPERs and teaches how to use the promoters. Applicant submits that the specification provides sufficient disclosure and enablement so that one skilled in the art could make the embodiments encompassed by the present claims. The instant specification provides primary DNA sequence, a working example of isolation technique (see Example 1 on page 26 of the specification), and detailed structural description (Figures 1 and 2) sufficient that one of skill in the art could make or use the invention as claimed. The level of specificity usually required for nucleotide claims is a recitation of the sequence of nucleotides that make up the DNA. Such a recitation is present in present claims 2-16. The functional limitation is that the sequence be

Serial No.: 09/766,399
Group Art Unit: 1634

"capable of driving transcription in a plant cell" as defined in the specification and discussed herein.

Examiner has stated that the specification does not provide any guidance as to how the elements can be rearranged and still result in a functional promoter. Applicant respectfully wishes to remind the Examiner, that the claims are drawn to the nucleotide sequence comprised of the specific promoter elements sequentially (claim 2(a)), and the sequence comprising SEQ ID NO: 65 (claim 2(b)) which is capable of driving transcription in a plant cell. Applicant is not claiming nucleotides comprising the promoter elements that are not arranged in the claimed sequential order. Also, the specification clearly shows the claimed SMPER sequences are capable of driving transcription in a plant cell.

In *In re Wands*, 858 F.2d 731 (Fed Cir.1988), it was stated "[w]hether undue experimentation is needed is not a single, simple fact determination, but rather is a conclusion reached by weighing many factual considerations." The court also gave the now well known 8 factors to help in this determination: "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." If these factors are applied to the present application and claims it is clear that undue experimentation is not required for one of skill in the art to identify promoters commensurate in scope with the instant claims as amended.

A person of skill in the art would not realistically set out to find every possible modification, nor is the Applicant required to supply such, as discussed above. It is only necessary that the specification teach a way to test whether a certain modification would work, which it does (Experiments 1 through 3, for example) The quantity of experiments necessary to determine if minor modifications are functional would not be large. In fact, Applicant demonstrated greater than 50% (9/17) success

Serial No.: 09/766,399
Group Art Unit: 1634

rate in the present application without knowing which promoter elements to use or in what frequency or in what order. Clearly, given the teachings of the instant application, one of skill in the art could make minor modifications to one or more of the promoter elements (claims 2d, 8d, and 12d) or add intervening sequences to the promoter elements for a total primer length up to 2000 nucleotides (claims 2a, 8a, and 12a) and test to see which ones drive transcription in a plant cell (as taught in Examples 3 and 4 of the present invention). Further, the amount of direction and guidance, as well as working examples, presented in the specification is clearly enough to enable this invention without undue experimentation. As to the nature of the invention and the state of the art in promoters or synthetic promoters, given the detail taught in the specification and the level of knowledge of promoters in general in the prior art, one of skill in the art would be able to practice the claimed invention without undue experimentation.

In regard to the state of the art and the predictability or unpredictability of the art, the level of one of skill in the art *at the time this application was filed* would have been of such a level that making minor modifications to a set of known promoter elements or adding intervening sequence between known promoter elements to arrive at a functional promoter would not have required undue experimentation. The Examiner points out that in *Genentech, Inc. v. Novo Nordisk*, 108 F.3d 1361 (Fed Cir. 1997), that where there is no disclosure of "any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art." The Examiner admits that Applicant provides the promoter elements of SEQ ID NO.: 65, but then goes on to state that without specific guidance as to *how to modify* the claimed sequences to produce a functional promoter would require undue experimentation. Applicants respectfully points out that in *Genentech*, the court was deciding, at least in part, whether the level of experimentation would

Serial No.: 09/766,399
Group Art Unit: 1634

be undue at the time the application was filed *in 1979*. Further, the court stated, "[w]here, as here, the claimed invention is the application of an unpredictable technology in the *early stages of development*, an enabling description in the specification must provide those skilled in the art with a specific and useful teaching." (emphasis added) Applicants respectfully submit that the Provisional Application 60/177,437 from which this application claims benefit was filed January 21, 2000. More than 20 years after the application of *Genentech*. One of skill in the art of recombinant DNA synthesis *in the year 2000* would clearly know to how make minor modifications to the promoter elements taught in the present application that would not have been unpredictable or require undue experimentation. However, the person of skill in the art is not required to make these modifications without any direction, as the present application is replete with teachings of how one of skill in the art could modify sequences (for example see pages 11 -14) and goes on to teach how one of skill in the art could test those modifications for functionality (See Examples 3 and 4, for example). Finally, the breadth of the claims as amended in the current application are commensurate with the teachings of the specification and with the skill of one of the art in recombinant DNA in the year 2000.

In light of the above, Applicant submits that the present invention as claimed is enabled and does not require undue experimentation. Applicant respectfully requests that the Examiner reconsider and withdraw the rejections to claims 2-16 under 35 U.S.C. §112, first paragraph.

The Section 102 Rejections of Claims 2-16: Anticipation by Ishige et al.

Claims 2-16 are rejected under 35 U.S.C. §102(b) as being anticipated by Ishige et al. (EP 0754757 A2). Examiner states that the teachings of Ishige et al. disclose a nucleotide sequence that hybridizes under stringent conditions to the

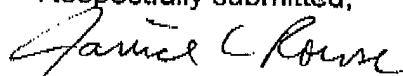
Serial No.: 09/766,399
Group Art Unit: 1634

nucleotide claimed in the instant application. The limitation providing stringent conditions are present in the claims, but not clearly defined as required by the Examiner. Examiner has stated that amendment of claims 2, 8 and 12 to include the language "wherein stringent conditions are" would obviate the art rejections. Applicant has amended claims 2, 8 and 12 to include the suggested language and in accordance with the Examiner's suggested remarks. Applicant respectfully requests that the rejections to claims 2-16 based on 35 U.S.C. 102 (b) be withdrawn.

SUMMARY

Applicant respectfully submits that in light of the foregoing amendments and remarks, claims 1-6 and 8-16 are in condition for allowance. Further examination, reconsideration and allowance of the claims are respectfully requested. If prosecution toward allowance could be furthered by a telephone call to the undersigned, one is earnestly requested.

Respectfully submitted,



Janice L. Rouse
Agent for Applicant(s)
Registration No. 52,183

PIONEER HI-BRED INTERNATIONAL, INC.
Corporate Intellectual Property
7100 N.W. 62nd Avenue
P.O. Box 1000
Johnston, Iowa 50131-1000
Phone: (515) 253-5707
Facsimile: (515) 334-6883